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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,340	11/20/2003	Rory F. Finn	01449/I	3646
45734 7590 04/03/2008 SENNIGER POWERS LLP (PIA) ONE METROPOLITAN SQUARE 16TH FLOOR ST. LOUIS, MO 63102				
EXAMINER AUDET, MAURY A				
ART UNIT		PAPER NUMBER		
1654				
NOTIFICATION DATE		DELIVERY MODE		
04/03/2008		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

### Office Action Summary

**Application No.**

10/718,340

**Applicant(s)**

FINN, RORY F.

**Examiner**

MAURY AUDET

**Art Unit**

1654

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-9, 15 and 21-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9, 15 and 21-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 November 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 2/11/08
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's amendment, response and filing of the RCE on 2/11/08 are acknowledged.

#### ***Election/Restrictions***

As noted before, Applicant's election with traverse, which was made Final, of Group I, claims 1-9 and 15, and the species m=3, n=4, and R=human growth hormone, in the reply filed on 09/18/2006 is maintained.

Claims 1-9, 15, and 21-24 are pending examined on the merits as being drawn to the elected invention, and the species m=3, n=4, and R=human growth hormone.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 15, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cunningham et al. (US 5,849,535) in view of Kinstler et al. (US 5,824,784).

The invention, in Applicant's words on specification para 27-28 is drawn to:

**[0025] The previous reports of PEGylated hGH require the attachment of multiple PEGs, which results in undesirable product heterogeneity, to achieve a hydrodynamic volume greater than the 70K molecular weight cut-off of the kidney filtration as described (Knauf, M.J. et al, J. Biol. Chem. 263:15064-15070,1988).**

**[0028] Therefore, it would be desirable to have a PEGylated hGH molecule that has a single PEG attached at a single site. The present invention addresses this need in a number of ways.**

Cunningham et al. expressly teach "*a composition containing a pegylated HGH variant for use in a therapeutic formulation can be heterogeneous or homogeneous, i.e., containing a single PEG-HGH form*" (col. 25, lines 7-9). Cunningham et al. does not expressly teach that the PEG has  $m=3$  and  $n=4$ , the presently elected species. Cunningham et al. also teach amino-terminal methionyl growth hormone (bovine strain) (col. 2, line 66). Cunningham et al. does not analyze whether either heterogeneous or homogeneous PEG-HGH's is better than the other, but as concerns the presently claimed products, such would not be relevant. The single PEG-HGH product, or equivalents thereof, are either taught or obvious thereof. Cunningham et al. does not expressly teach that the mPEG has a molecular weight of about 20 kDa.

Kinstler et al. teach the conjugation of mono-N-terminal mPEG-peptide conjugates, wherein mPEG has a molecular weight of about 20 kDa (Fig. 9).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make the presently elected single, homogenous PEG-HGH conjugate wherein  $m=3$ , and  $n=4$ , in Cunningham et al., because the reference advantageously and

expressly teach the desired results Applicant was driving for: a single PEG conjugate to an HGH to obtain homogeneity. The modification of  $m$  to 3 and  $n$  to 4, the elected species, is a known PEG compound, absent evidence to the contrary. The present description did not indicate any unexpected results bearing this combination over any other variant of PEG, absent evidence to the contrary. PEG being one of the most highly modified and routinely optimized peptide linked molecules of modern day chemistry, the attachment of this or any known PEG compound at the time of the invention, in singular form, at a single position of HGH (e.g. at the well-known attachment site of the N-terminus), is deemed *prima facie* obvious. Absent some showing of unexpected results through evidentiary testing, by one singularly attached form of PEG to HGH, versus other singularly attached PEG-HGH forms. Similarly, the use of known methionyl HGH as opposed to native HGH or any other analog thereof, known at the time of the invention would have been merely a matter of routine optimization.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make the presently elected single, homogenous PEG-HGH conjugate wherein  $m=3$ , and  $n=4$ , wherein the mPEG has a molecular weight of about 20 kDa, in Cunningham et al., because Kinstler et al. advantageously teach the conjugation of mono-N-terminal mPEG-peptide conjugates, wherein mPEG has a molecular weight of about 20 kDa (Applicant's claims 23-24). The use of the known mPEG at a 20 kDa weight for like-kind conjugates with another peptide (HGH) would have merely been a matter of routine optimization by the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 8/28/2007

/Maury Audet/  
Examiner, Art Unit 1654